

**Amendments to the Specification:**

*Please replace the paragraph beginning at page 2, line 1 with the following amended paragraph:*

The advent of green fluorescent protein (GFP) as a reporter molecule provided several advantages in screening and identifying cells expressing the heterologous gene. Co-expression of GFP enables real-time analysis and sorting of transfectants by fluorescence without the requirement of additional substrates or cofactors and without destroying the cell sample. The use of GFP as a reporter molecule to monitor gene transfer has been described in various publications. Chalfie *et al.* in U.S. Patent No. 5,491,084 describe a method of selecting cells expressing a protein of interest that involves co-transfecting cells with one DNA molecule containing a sequence encoding a protein of interest, and a second DNA molecule which encodes GFP, then selecting cells which express GFP. Gubin *et al.*, in *Biochem. Biophys. Res. Commun.* 236: 347-350 (1997) describe transfection of CHO cells with a plasmid encoding GFP and neo to study the stable expression of GFP in the absence of selective growth conditions. Mosser *et al.*, *Biotechnology* 22: 150-[[154]]161 (1997) describe the use of a plasmid containing a dicistronic expression cassette encoding GFP and a target gene, in a method of screening and selection of cells expressing inducible products. The target gene was linked to a controllable promoter. The plasmid incorporates a viral internal ribosome entry site (IRES) to make it possible to express a dicistronic mRNA encoding both the GFP and a protein of interest. This plasmid described by Mosser does not contain any selectable gene; the selectable gene is provided in a separate plasmid which is transfected sequentially or co-transfected with the GFP/target gene-encoding plasmid. This expression system lacks spatial and transcriptional linkage between the gene of interest, the drug selectable marker and GFP. Levenson *et al.*, *Human Gene Therapy* 9:1233-1236 (1998) describe retroviral vectors containing a single promoter followed by a multiple cloning site, a viral internal ribosome entry site (IRES) sequence and a selectable marker gene. The selectable markers used were those that conferred resistance to G418, puromycin, hygromycin B, histidinol D, and phelomycin, and also included GFP.

*Please replace the paragraph beginning at page 8, line 24 with the following amended paragraph:*

Figure 20 shows the nucleic acid sequence of a vector comprising two promoters from SV40, the puromycin/DHFR fusion gene, and two sites for insertion of two heterologous proteins (SEQ ID NO:15).

The structure of the vector is analogous to the structure shown in Figure 21, but without specific heterologous polypeptides inserted into the vector.

*Please replace the paragraph beginning at page 8, line 31 with the following amended paragraph:*

Figure 22 shows the nucleotide sequence of the vector of Figure 21 (SEQ ID NO:16).

*Please replace the paragraph beginning at page 8, line 34 with the following amended paragraph:*

Figure 24 shows the nucleotide sequence of the vector of Figure 23 (SEQ ID NO:17).

*Please replace the paragraph beginning at page 12, line 22 with the following amended paragraph:*

For references directed to co-transfection of a gene together with a genetic marker that allows for selection and subsequent amplification, see, *e.g.*, Kaufman in Genetic Engineering, ed. J. Setlow (Plenum Press, New York), Vol. 9 (1987); Kaufman and Sharp, *J. Mol. Biol.*, 159:601 (1982); Ringold *et al.*, *J. Mol. Appl. Genet.*, 1:165-175 (1981); Kaufman *et al.*, *Mol. Cell Biol.*, 5:1750-1759 (1985); Kaetzel and Nilson, *J. Biol. Chem.*, 263:6244-6251/6344-6351 (1988); Hung *et al.*, *Proc. Natl. Acad. Sci. USA*, 83:261-264 (1986); Kaufman *et al.*, *EMBO J.*, 6:87-93/187-193 (1987); Johnston and Kucey, *Science*, 242:1551-1554 (1988); Urlaub *et al.*, *Cell*, 33:405-412 (1983). For a review of the amplifiable selectable genes listed in Table 1, see Kaufman, *Methods in Enzymology*, 185: 537-566 (1990).

*Please replace the paragraph beginning at page 25, line 19 with the following amended paragraph:*

DHFR, the desired protein and GFP can be expressed from one promoter to improve the co-expression efficiency. For example, GFP and DHFR can be expressed as a fusion protein, or an IRES can obviate the need for a second promoter to express GFP. In the constructs shown in Figure [[9]]1, rows 1 and 2, the exemplary amplifiable selectable gene, DHFR, is fused to the GFP gene to form a DHFR-GFP fusion gene. Each of the upstream and downstream coding sequences (in the first example in Figure [[9]]1, row 1, the upstream coding sequence is DHFR-GFP fusion gene; in the second example represented in row 2, the upstream coding sequence is the selected sequence) has its translational stop signal. Translation initiates again for the downstream coding sequence. These scenarios allow expression of two separate proteins from a single promoter. It will be understood that the positioning of the promoter/enhancer, translational stop signal, translational initiation site, transcription termination site and polyA signal, relative to the various components in each transcription unit, as described here, apply to all the constructs described below.

*Please replace the paragraph beginning at page 27, line 34 with the following amended paragraph:*

The constructs of the invention can also comprise two expression/transcription units, as shown in Figure [[9]]1, rows 4-9. The two-transcription unit construct depicted in Figure [[9]]1, row 4, comprises one selected sequence. Rows 5-9 show constructs wherein two selected sequences can be inserted, one in each transcription unit. Each of the two transcription units will comprise a promoter and optionally, an enhancer, a transcriptional termination site and polyA signal sequence. The second transcription unit can use the same or different kind of promoter as used in first transcription unit. For example, both transcription units can use the SV40 promoter. One or both of the transcription units can comprise an intron.

*Please replace the paragraph beginning at page 28, line 3 with the following amended paragraph:*

Figure [[9]]1, row 4, illustrates a construct wherein the first transcription unit contains DHFR in an intron (the first intron), followed by the selected sequence. The second transcription unit will comprise the GFP gene. The second transcription unit will preferably comprise an intron (referred to as the second intron) immediately 5' of the GFP. The three coding sequences are still physically linked in one vector but are independently transcribed from two promoters. The primary transcript produced from the first transcription unit encodes both DHFR and the selected sequence but only the DHFR gene is translated into product. Preferably, at least 95% of the transcripts will have the DHFR gene spliced out and will translate into the desired product. In the second transcription unit, if the GFP is placed downstream of an intron, both spliced and unspliced transcripts from this transcription unit will produce GFP.

*Please replace the paragraph beginning at page 28, line 19 with the following amended paragraph:*

In yet another embodiment of the preceding construct comprising two transcription units and two introns, instead of placing the GFP gene within the second intron in the second transcription unit, an IRES is placed between the second selected sequence and the GFP gene (Fig. [[9]]1, row 6). Both the second selected sequence and the GFP gene from the second transcription unit will be translated from the dicistronic message.

*Please replace the paragraph beginning at page 28, line 28 with the following amended paragraph:*

In still another variation of the construct comprising two-transcription units and two introns, the first intron in the first transcription unit is left empty but an IRES is inserted downstream of the first gene

of interest to allow translation of a downstream DHFR-GFP fusion gene. The second transcription unit will comprise the second intron followed by a second gene of interest (Fig. [[9]]1, row 8). Optionally, another selectable marker gene (other than the amplifiable selectable gene and GFP gene), can be placed within the second intron or the intron can remain without an inserted gene.